Technical Information Bulletin

U.S. Department of Labor
Occupational Safety and Health Administration

Potential Health Hazards Associated with the Process of Compounding Medications from Pharmaceutical Grade Ingredients.

TIB 01-12-21

Purpose

The purpose of this Technical Information Bulletin (TIB) is both to inform and remind the pharmaceutical industry, its employees, and the health care community, of the potential hazards of compounding medications, including "potent compounds" which contain hazardous drugs.

Background

Compounding facilities specialize in preparing custom ordered medications prescribed for patients by a licensed physician or practitioner. Medications may be compounded at a variety of settings, such as a community based pharmacy on a case-by-case basis, or at a hospital based pharmacy for use in specific treatments or procedures.

Although the intent of compounding medications is to benefit patients therapeutically, the ingredients used in these medications may present occupational hazards to the workers compounding them. Pharmacists, nurses, technicians, and others who prepare, handle and administer these medications may be exposed to significant health risks during the course of their work. Hazardous exposure to workers may occur through inhalation of dust created during: hand manipulation; operation of a tablet encapsulation machine; and by performing sieving and granulation operations, particularly when appropriate engineering controls are not applied. Dermal absorption may occur when preparing creams, liquids, gels, and moisturizers. Improper handling of these medications may contaminate the environment (e.g., keyboards, tabletops, waste baskets) and may produce deleterious health effects, both acute and chronic, in exposed workers. Potent compounds can be carried home on workers' clothing posing a potential hazard to workers' families as well. Although the greatest risk is to workers who are compounding these medications, people in adjacent work areas (e.g., clerical workers, support staff, maintenance personnel, and visitors) also may be at risk of exposure which can occur through inhalation of "fugitive" drug aerosols, or by contact with contaminated surfaces and floors.

There are many examples of medications that can be hazardous when compounded. Three common examples that may present significant risks to the compounder include:

A. custom preparations of specific antineoplastics (anticancer drugs), such as ointments compounded with busulfan intended for use as external skin treatments;

B. compounded hormone medications using specialized dosage forms, such as creams, lozenges, suppositories, capsules, tablets, or gels. Compounded hormone prescriptions may include hazardous ingredients, such as the hormones progesterone, testosterone, methyl testosterone, estradiol, and estriol;

C. certain forms of antibiotics, such as penicillin, that when compounded may pose the threat of serious allergic reactions. Proper precautiions should be taken by individuals allergic to the penicillin class of drugs to minimize or eliminate exposure when in a facility that is compounding penicillin class products.

A number of studies referenced in the *OSHA Technical Manual for Controlling Occupational Exposure to Hazardous Drugs* (Section Vl: Chapter 2), and the American Society of Health System Pharma*cists (ASHP)* Technical Assistance Bulletin on *Handling Cytotoxic and Hazardous Drugs* have examined the potential health effects of occupational exposure to antineoplastic drugs. The information available suggests that exposure may lead to possible chromosomal aberrations, congenital malformations, nausea, dizziness, and allergic reactions, indicating that employee exposure to antineoplastic drugs should be limited to the extent feasible.

Studies have also been undertaken to assess the health effects of occupational exposure to hormones. Acute health problems have been reported among exposed workers, including menstruation anomalies (e.g., irregular bleeding), and possible testicular dysfuction. Unwanted changes in physical appearance, such as masculinization of female workers and breast development in males also have been reported. An increase in breast cancer has also been reported, which may be attributed to inhalation and skin absorption of estrogen during work. Although further research is needed in this area to draw definitive conclusions on the long-term effects of continued exposure to small amounts of such drugs, some of the present studies suggest that a number of these hormones may produce a variety of adverse effects (e.g., cancer, impaired fertility). (*Scandinavian J. Work, Environ Health 8* (1982), Supplement 1, 167-171; Material Safety Data Sheet (MSDS) for Testoterone, April 29, 1998; MSDS for Estradiol, April 1, 1996; *International Journal of Epidemiology,*1994), Vol 22, No. 5, 891-898; ASHP, Technical Assistance Bulletin on *Handling Cytotoxic and Hazardous Drugs).*

Potent compounds have been recognized as an occupational hazard since the 1980's. In1995, OSHA updated guidelines and recommendations in its *Technical Manual*, Controlling Occupational Exposure to Hazardous Drugs (Section VI, Chapter 2) (available on line at www.osha-slc.gov/dts/osta/otm/otm_toc.html). This chapter has information on the OSHA Hazard Communication Standard (29 CFR 1910.1200), as well as the categorization of specific drugs as "hazardous drugs", a discussion of hazardous drugs as occupational risks, and the prevention of employee exposures through the use of engineering controls, personal protective equipment, and work practices. In the 1980's and early 1990's, several other organizations published recommendations for policies and procedures related to the occupational risks associated with anticancer agents in the health care setting. Some of these organizations include: the American Society of Health System Pharmacists (ASHP); the Oncology Nursing Society; the Council on Scientific Affairs of the American Medical Association; the National Study Commission on Cytotoxic Exposure; and the Canadian Society of Hospital Pharmacists (see, e.g., *Am J. Health-Syst. Pharm.*, Vol. 56, Jul 15, 1999).

Additional data on toxicity of certain drugs were obtained in response to a Federal Register notice issued by the Food and Drug Administration (FDA) in April 1998, requesting nominations from the public for a list of bulk drug substances to be used in pharmacy compounding. The FDA and the Pharmacy Compounding Advisory Committee noted that the following drug substances pose potential hazards to persons handling them: cantharidin, dinitrochlorobenzene, hydrazine sulphate, diphenylcyclopropenone, and squaric acid dibutyl ester (Proposed Rule, *Federal Register*; Vol. 64. No. 4, January 7, 1999).

The potential hazards from exposure to compounded medications are also recognized and referenced in scientific journal articles, Material Safety Data Sheets, pharmacological textbooks, the *Physician's Desk Reference*, documents from specific pharmaceutical manufacturers, the *U.S. Pharmacopoeia* (U.S.P), and

in the monthly updated publication *Drug Facts and Comparisons*. These references contain information on exposure limits, and recommend good-practices for the compounding of medications. They also describe proper sampling methods, as well as specifying carcinogenic classifications.

Recommendations

Individuals in health care and pharmaceutical settings should be aware of the hazards of exposure to ingredients during the compounding, handling and administering of compounded medications. Employers should determine if their workers are at risk of exposure to hazards associated with compounded medications. Specific measures should be implemented to: reduce direct skin contact; reduce exposure via inhalation; and minimize the possibility of chemicals being brought home on workers' clothing. As with all potentially hazardous exposures, protective measures should include: engineering controls (e.g., barriers and containments, laboratory hoods, glove boxes, and worker isolation); administrative controls; personal protective equipment (e.g., respirators, gloves and lab coats); and training.

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